

NOVEL MODULATORS OF AMYLOID-BETA PRODUCTION AND USES THEREOF

Abstract of the Disclosure

[00173] The present invention provides isolated nucleic acid sequences encoding presenilin stabilization factor (PSF) and PSF-like (PSFL) protein, vectors comprising same, 5 host cells transformed with the vectors, and transgenic animals containing the host cells. The present invention further provides purified PSF and PSFL polypeptides, methods for making same, and pharmaceutical compositions comprising the polypeptides. Also provided are agents reactive with the nucleic acid sequences and polypeptides, kits comprising same, and methods for producing same. The present invention further provides methods for decreasing 10 amyloid-beta (A $\beta$ ) production, destabilizing presenilin or nicastrin, destabilizing a gamma-secretase complex, and inhibiting activity of gamma-secretase, and pharmaceutical compositions for accomplishing same. The present invention further provides methods for treating neurodegeneration in a subject. Finally, the present invention provides an *in vitro* system for identifying an agent that modulates production of A $\beta$  or an A $\beta$  precursor, methods 15 for making and using same, and agents identified by same.